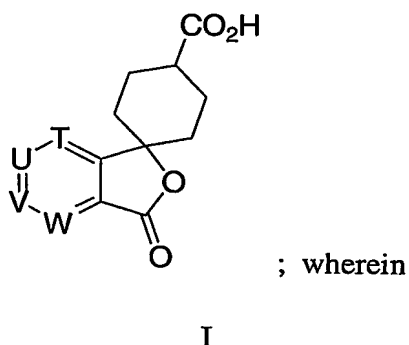


## WHAT IS CLAIMED IS:

1. A process for preparing a compound of the formula I, or a salt thereof



T, U, V and W are each independently selected from the group consisting of

- (1) nitrogen, and
- (2) methine,

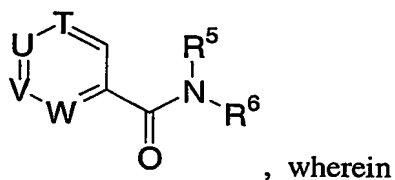
wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy, and

wherein at least two of T, U, V, and W are methine;

comprising the steps of

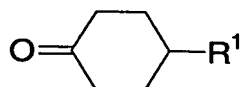
- (a) combining a strong base with a compound of formula III



R<sup>5</sup> and R<sup>6</sup> are independently selected from the group consisting of

- (1) hydrogen,
- (2) lower alkyl,

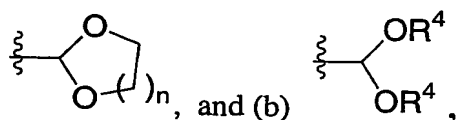
- (3) cycloalkyl,
  - (4) cycloheteroalkyl,
  - (5) aryl, and
  - (6) heteroaryl,
- in an aprotic solvent to form a solution;
- (b) reacting a cyclohexanone of formula IV with the solution of step (a)



IV

wherein R<sup>1</sup> is selected from the group consisting of

- (1) -CO<sub>2</sub>H,
- (2) -CN,
- (3) -CH<sub>2</sub>OH,
- (4) aryl,
- (5) ester,
- (6) protected carboxylic acid, and
- (7) a ketal selected from the group consisting of



- wherein n is 1 or 2, and R<sup>4</sup> is lower alkyl;
- (c) converting the R<sup>1</sup> substituent of step (b) into a carboxylic acid when R<sup>1</sup> is not a carboxylic acid; and
  - (d) adding an acid to form a spirolactone;
- to afford the compound I, or a salt thereof.

2. The process of Claim 1 further comprising the step (e) of isolating the compound of formula I.

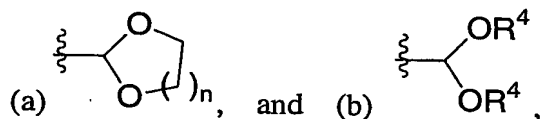
3. The process of Claim 1 step (b) wherein R<sup>1</sup> is selected from the group consisting of:

- (1) -CO<sub>2</sub>H,

- (2)  $-\text{CN}$ ,
- (3)  $-\text{CH}_2\text{OH}$ ,
- (4) phenyl,
- (5)  $-\text{CO}_2\text{R}^2$ , wherein  $\text{R}^2$  is selected from the group consisting

of:

- (a) lower alkyl, and
- (b)  $-\text{CH}_2\text{-phenyl}$ , wherein the phenyl group is unsubstituted or substituted with a substituent selected from the group consisting of:
  - (1) lower alkyl,
  - (2) lower alkoxy, and
  - (3)  $-\text{NO}_2$ ,
- (6)  $-\text{C}(\text{O})\text{NHR}^3$ , wherein  $\text{R}^3$  is lower alkyl,
- (7)  $-\text{C}(\text{O})\text{N}(\text{R}^3)_2$ , wherein  $\text{R}^3$  is lower alkyl,
- (8)  $-\text{C}(\text{O})\text{NH}_2\text{NH}_2$ , and
- (9) a ketal selected from the group consisting of



wherein  $n$  is 1 or 2, and  $\text{R}^4$  is lower alkyl.

4. The process of Claim 3 wherein wherein  $\text{R}^1$  is  $-\text{CO}_2\text{R}^2$ , wherein  $\text{R}^2$  is selected from the group consisting of:

- (a) lower alkyl, and
- (b)  $-\text{CH}_2\text{-phenyl}$ , wherein the phenyl group is unsubstituted or substituted with a substituent selected from the group consisting of:
  - (1) lower alkyl,
  - (2) lower alkoxy, and
  - (3)  $-\text{NO}_2$ .

5. The process of Claim 1 wherein T, V and W are methine, wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy; and

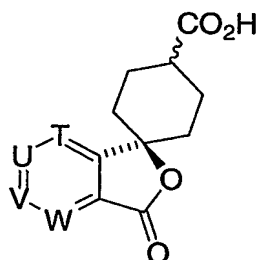
U is nitrogen.

6. The process of Claim 5 wherein T, V and W are unsubstituted methine; and U is nitrogen.

7. The process of Claim 1 wherein T, U, V and W are methine, wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy.

8. A process for preparing a compound of the formula IC, or a salt thereof,



IC

; wherein

T, U, V and W are each independently selected from the group consisting of

- (1) nitrogen, and
- (2) methine,

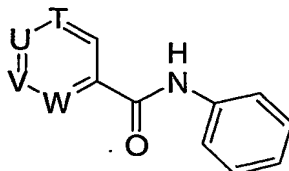
wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and

(d) lower alkoxy, and  
wherein at least two of T, U, V, and W are methine;

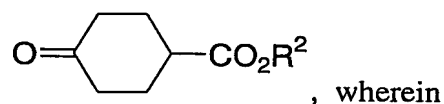
comprising the steps of

(a) combining a strong base with a compound of formula A



A

in an aprotic solvent to form a solution;  
(b) reacting a compound of formula B



B

R<sup>2</sup> is selected from the group consisting of:

- (a) lower alkyl, and
- (b) -CH<sub>2</sub>-phenyl, wherein the phenyl group is  
unsubstituted or substituted with a substituent selected from the group  
consisting of
  - (1) lower alkyl,
  - (2) lower alkoxy, and
  - (3) -NO<sub>2</sub>,

with the solution of step (a) to form a solution;

- (c) reacting the solution of step (b) with water to form a solution; and
- (d) adjusting the pH of the solution of step (c) to between about 0 and 4 with an acid to afford the compound IC, or a salt thereof.

9. The process of Claim 8 further comprising the step (e) of isolating the compound of formula IC, or a salt thereof.

10. The process of Claim 8 wherein steps (a) and (b) are run at a temperature of between about  $-50^{\circ}\text{C}$  and  $-80^{\circ}\text{C}$ .

11. The process of Claim 8 wherein the aprotic solvent of step (a) is selected from the group consisting of tetrahydrofuran, toluene, heptane, dimethoxyethane, benzene, and hexane, diethyl ether, xylene, or a mixture thereof.

12. The process of Claim 11 wherein the aprotic solvent of step (a) is tetrahydrofuran.

13. The process of Claim 8 wherein the strong base of step (a) is selected from the group consisting of n-BuLi, sec-BuLi, t-BuLi, LiHMDS, NaHMDS, KHMDS and LiTMP.

14. The process of Claim 13 wherein the strong base of step (a) is n-BuLi.

15. The process of Claim 8 wherein step (a) further comprises adding a salt selected from the group consisting of LiBr, LiCl, LiI, LiBF<sub>4</sub>, LiClO<sub>4</sub>, and CeCl<sub>3</sub>.

16. The process of Claim 15 wherein the salt of step (a) is LiBr.

17. The process of Claim 8 wherein R<sup>2</sup> is selected from the group consisting of  $-\text{CH}_3$ ,  $-\text{CH}_2\text{CH}_3$ ,  $-(\text{CH}_2)_2\text{CH}_3$ ,  $-\text{CH}(\text{CH}_3)_2$ ,  $-(\text{CH}_2)_3\text{CH}_3$ , and  $-\text{CH}(\text{CH}_3)_3$ .

18. The process of Claim 17 wherein R<sup>2</sup> is  $-\text{CH}_2\text{CH}_3$ .

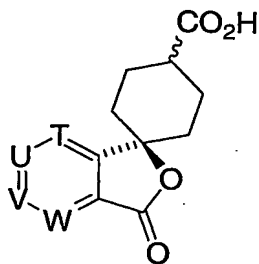
19. The process of Claim 8 wherein the acid of step (d) is selected from the group consisting of hydrochloric acid, sulfuric acid, methane sulfonic acid, trifluoromethane sulfonic acid, and or a mixture thereof.

20. The process of Claim 19 wherein the acid of step (d) is

sulfuric acid.

21. The process of Claim 8 further comprising the steps of

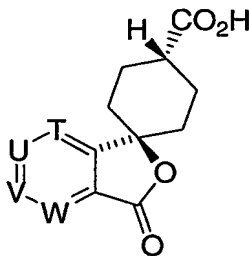
(f) adding an aprotic solvent to the compound of formula IC, or a salt thereof,



IC

to form a mixture; and

(g) aging the mixture of step (f) for a time and under conditions effective to afford the compound IA, or a salt thereof,



IA

22. The process of Claim 21 wherein the aprotic solvent of step (f) is selected from the group consisting of tetrahydrofuran, ethyl acetate, methyl *t*-butyl ether, toluene, or a mixture thereof.

23. The process of Claim 21 wherein step (f) further comprises adding an acid to the mixture of step (f).

24. The process of Claim 23, wherein the acid of step (f) is selected

from the group consisting of hydrochloric acid, hydrobromic acid, tartaric acid, methane sulfonic acid, toluene sulfonic acid, succinic acid, and sulfuric acid.

25. The process of Claim 24 wherein the acid of step (f) is hydrochloric acid.

26. The process of Claim 21, wherein step (g) is aged at a temperature of about 40°C to 60°C.

27. The process of Claim 21, further comprising the step (h) of isolating the compound of formula IA, or a salt thereof.

28. The process of Claim 8 wherein T, V and W are methine, wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy; and

U is nitrogen.

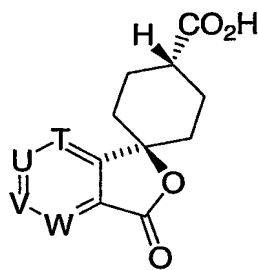
29. The process of Claim 28 wherein T, V and W are unsubstituted methine; and U is nitrogen.

30. The process of Claim 8 wherein T, U, V and W are methine, wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy.

31. A process for preparing a compound of the formula IA, or a salt thereof,





; wherein

IA

T, U, V and W are each independently selected from the group consisting of

- (1) nitrogen, and
- (2) methine,

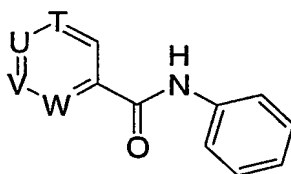
wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy, and

wherein at least two of T, U, V, and W are methine;

comprising the steps of

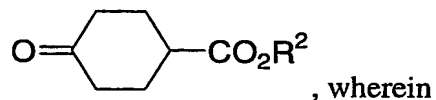
- (a) combining a strong base with a compound of formula A



A

in an aprotic solvent to form a solution;

- (b) reacting a compound of formula B



, wherein

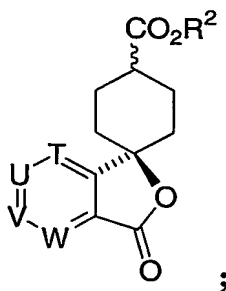
B

wherein  $R^2$  is selected from the group consisting of:

- (a) lower alkyl, and
- (b)  $-\text{CH}_2\text{-phenyl}$ , wherein the phenyl group is unsubstituted or substituted with a substituent selected from the group consisting of
  - (1) lower alkyl,
  - (2) lower alkoxy, and
  - (3)  $-\text{NO}_2$ .

with the solution of step (a) to form a solution;

- (c) adjusting the pH of the solution of step (b) to between about 0 and 4 with an acid to form a compound of formula E



E

- (d) contacting the compound of formula E of step (c), wherein at least one of T, U, V and W is nitrogen, with an acid to form a salt of compound E; and
- (e) treating compound E, or a salt thereof, with an acid to form a salt of compound IA.

32. The process of Claim 31 wherein steps (a) and (b) are run at a temperature of between about  $-50^{\circ}\text{C}$  and  $-80^{\circ}\text{C}$ .

33. The process of Claim 31 wherein the aprotic solvent of step (a) is selected from the group consisting of tetrahydrofuran, toluene, heptane, dimethoxyethane, benzene, and hexane, diethyl ether, xylene, or a mixture thereof.

34. The process of Claim 33 wherein the aprotic solvent of step (a) is tetrahydrofuran.
35. The process of Claim 31 wherein the strong base of step (a) is selected from the group consisting of n-BuLi, sec-BuLi, t-BuLi, LiHMDS, NaHMDS, KHMDS and LiTMP.
36. The process of Claim 35 wherein the strong base of step (a) is n-BuLi.
37. The process of Claim 31 wherein step (a) further comprises adding a salt selected from the group consisting of LiBr, LiCl, LiI, LiBF<sub>4</sub>, LiClO<sub>4</sub>, and CeCl<sub>3</sub>.
38. The process of Claim 37 wherein the salt of step (a) is LiBr.
39. The process of Claim 31 wherein the acid of step (c) is selected from the group consisting of camphor sulfonic acid, sulfuric acid, hydrochloric acid, methane sulfonic acid, acetic acid, trifluoromethane sulfonic acid, or a mixture thereof.
40. The process of Claim 39 wherein the acid of step (c) is acetic acid.
41. The process of Claim 31 wherein step (c) further comprises adding a solvent selected from the group consisting of C<sub>1-6</sub> alcohol, tetrahydrofuran and toluene.
42. The process of Claim 41 wherein the solvent of step (c) is ethanol.
43. The process of Claim 31 wherein the acid of step (d) is selected from the group consisting of camphor sulfonic acid, sulfuric acid, hydrochloric acid, methane sulfonic acid, trifluoromethane sulfonic acid, or a mixture thereof.
44. The process of Claim 43 wherein the acid of step (d) is camphor sulfonic acid.

45. The process of Claim 31 wherein step (d) is heated to a temperature of between about 50°C to 80°C to form the salt.
46. The process of Claim 31 wherein R<sup>2</sup> is selected from the group consisting of: -CH<sub>3</sub>, -CH<sub>2</sub>CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, -CH(CH<sub>3</sub>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, and -CO<sub>2</sub>CH(CH<sub>3</sub>)<sub>3</sub>.
47. The process of Claim 46 wherein R<sup>2</sup> is -CH<sub>2</sub>CH<sub>3</sub>.
48. The process of Claim 31 wherein the acid of step (e) is selected from the group consisting of hydrochloric acid, sulfuric acid, methane sulfonic acid, trifluoromethane sulfonic acid, or a mixture thereof.
49. The process of Claim 48 wherein the acid of step (e) is sulfuric acid.
50. The process of Claim 31 wherein the temperature of step (e) is between about 50 °C and 100 °C.
51. The process of Claim 31 further comprising the step (f) of treating the salt of compound IA with a base to form free acid IA in solution.
52. The process of Claim 51 wherein the base of step (f) is selected from a group consisting of sodium hydroxide, potassium hydroxide, potassium carbonate, sodium carbonate, and sodium bicarbonate.
53. The process of Claim 52 wherein the base of step (f) is sodium hydroxide.
54. The process of Claim 53 further comprising the step (g) of isolating the compound of formula IA.
55. The process of Claim 31 wherein T, V and W are methine, wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy; and

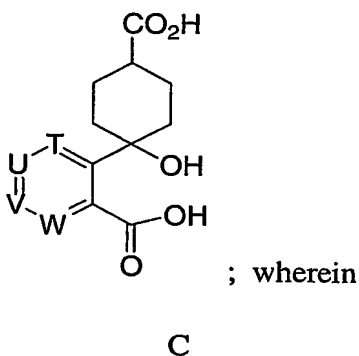
U is nitrogen.

56. The process of Claim 55 wherein T, V and W are unsubstituted methine; and U is nitrogen.

57. The process of Claim 31 wherein T, U, V and W are methine, wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy.

58. A compound of structural formula C, or a salt thereof,



; wherein

T, U, V and W are each independently selected from the group consisting of

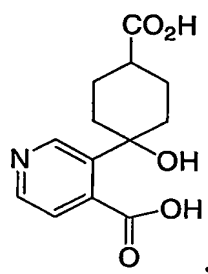
- (1) nitrogen, and
- (2) methine,

wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and

(d) lower alkoxy, and  
wherein at least two of T, U, V, and W are methine.

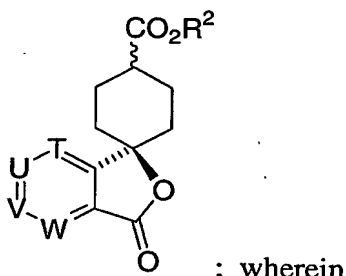
59. The compound of structural formula 1-3



1-3

or a salt thereof.

60. A compound of structural formula E, or a salt thereof,



; wherein

E

T, U, V and W are each independently selected from the group consisting of

- (1) nitrogen, and
- (2) methine,

wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy, and

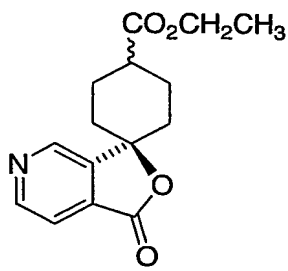
wherein at least two of T, U, V, and W are methine; and

R<sup>2</sup> is selected from the group consisting of:

- (a) lower alkyl, and
- (b) -CH<sub>2</sub>-phenyl, wherein the phenyl group is unsubstituted or substituted with a substituent selected from the group consisting of:
  - (1) lower alkyl,
  - (2) lower alkoxy, and
  - (3) -NO<sub>2</sub>.

61. The compound of Claim 58 wherein R<sup>2</sup> is selected from the group consisting of -CH<sub>3</sub>, -CH<sub>2</sub>CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>, -CH(CH<sub>3</sub>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>, and -CH(CH<sub>3</sub>)<sub>3</sub>.

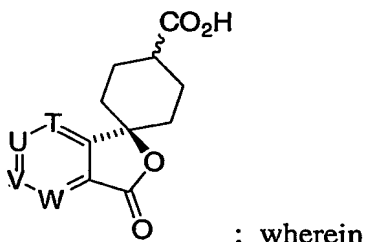
62. A compound of formula 2-3



2-3

or a salt thereof.

63. A process for preparing a compound of formula IC, or a salt thereof,



; wherein

IC

T, U, V and W are each independently selected from the group consisting of

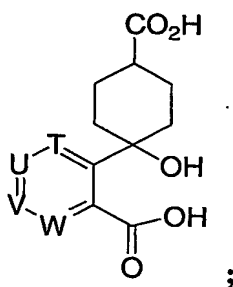
- (1) nitrogen, and
- (2) methine,

wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy, and

wherein at least two of T, U, V, and W are methine;

comprising the step of adjusting the pH of a solution of compound C



C

in a solvent to a pH between about 0 and 4 with an acid to afford the compound IC, or a salt thereof.

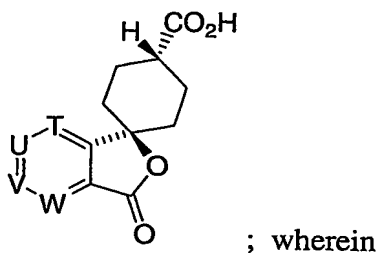
64. The process of Claim 63 wherein the solvent is selected from the group consisting of tetrahydrofuran, toluene, heptane, dimethoxyethane, benzene, and hexane, diethyl ether, xylene, water, or a mixture thereof.

65. The process of Claim 63 wherein the acid is selected from the group consisting of hydrochloric acid, sulfuric acid, methane sulfonic acid, trifluoromethane sulfonic acid, or a mixture thereof.

66. The process of Claim 63 further comprising isolating the compound of formula IC, or a salt thereof.

67. A process for preparing the compound of formula IA, or a salt thereof,





IA

T, U, V and W are each independently selected from the group consisting of

- (1) nitrogen, and
- (2) methine,

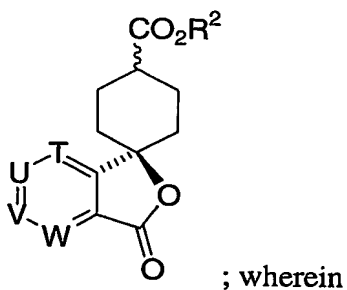
wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

- (a) halogen,
- (b) lower alkyl,
- (c) hydroxy, and
- (d) lower alkoxy, and

wherein at least two of T, U, V, and W are methine,

comprising the steps of

- (a) contacting the compound of formula E



E

R<sup>2</sup> is selected from the group consisting of:

- (a) lower alkyl, and
- (b) -CH<sub>2</sub>-phenyl, wherein the phenyl group is

unsubstituted or substituted with a substituent selected from the group consisting of

- (1) lower alkyl,
- (2) lower alkoxy, and
- (3)  $-\text{NO}_2$ , and

wherein at least one of T, U, V and W is nitrogen,

with an acid to form a salt of compound E; and

- (b) treating compound E, or a salt thereof, with an acid to form compound IA, or a salt thereof.

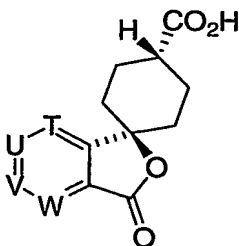
68. The process of Claim 67 wherein the acid of step (a) is selected from the group consisting of camphor sulfonic acid, sulfuric acid, hydrochloric acid, methane sulfonic acid, trifluoromethane sulfonic acid, or a mixture thereof.

69. The process of Claim 67 wherein  $\text{R}^2$  is selected from the group consisting of:  $-\text{CH}_3$ ,  $-\text{CH}_2\text{CH}_3$ ,  $-(\text{CH}_2)_2\text{CH}_3$ ,  $-\text{CH}(\text{CH}_3)_2$ ,  $-(\text{CH}_2)_3\text{CH}_3$ , and  $-\text{CH}(\text{CH}_3)_3$ .

70. The process of Claim 67 wherein the acid of step (b) is selected from the group consisting of hydrochloric acid, sulfuric acid, methane sulfonic acid, trifluoromethane sulfonic acid, or a mixture thereof.

71. The process of Claim 67 further comprising the step (c) of isolating compound IA, or a salt thereof.

72. A process for preparing a compound of formula IA, or a salt thereof,



; wherein

IA

T, U, V and W are each independently selected from the group consisting of

(3) nitrogen, and

(4) methine,

wherein the methine group is unsubstituted or optionally substituted with a substituent selected from the group consisting of

(e) halogen,

(f) lower alkyl,

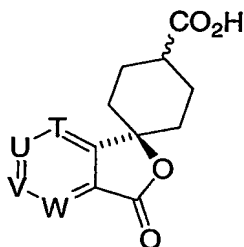
(g) hydroxy, and

(h) lower alkoxy, and

wherein at least two of T, U, V, and W are methine;

comprising the steps of

(a) adding an aprotic solvent to the compound of formula IC, or a salt thereof,



IC

to form a mixture; and

(b) aging the mixture of step (a) for a time and under conditions effective to afford the compound IA, or a salt thereof.